REMARKS

The instant disclosure and the Figures have been objected to on formal grounds. Pending claims 1-7 have been rejected for indefiniteness and lack of enablement and as anticipated by Li et al. These rejections are respectfully traversed for the reasons given below and reconsideration is requested.

Correction to the Specification and the Figures

Applicants have amended the specification herewith, as requested by the Examiner, to remove the embedded hyperlinks at p. 6, lines 9 and 12. Applicants submit that these calculation tools are not required given that the information obtained thereby is presented in the indicated figures.

Applicants acknowledge the Examiner's request for sequence identifiers at p. 22, lines 20 and 21. Applicants point out that the indicated sequences are for primers for PCR sequencing and are not part of the invention itself. These sequences were accidentially omitted in the original Sequence Listing submission. Applicants acknowledge their responsibility to correct the Sequence Listing and amend the specification accordingly. A corrected Sequence Listing will be submitted shortly.

The Examiner has objected to Figures 3A-3D for containing amino acid sequences in which the amino acids are designated by three lower case letters instead of using the one upper case letter convention, which is now considered standard. The Applicants will submit the appropriate replacement Figures shortly.

Rejection under 35 U.S.C. § 112, 2nd paragraph

Claims 1 and 4-5 have been rejected as indefinite in reciting the phrase "a therapeutically active portion," the Examiner saying that it is unclear what constitutes the therapeutic activity. Applicants point the Examiner to pp. 2-5 of the specification, where it is described that the lysyl oxidase pro-peptide active lysyl oxidase capacity shown by portion retains the expression of inhibiting the transforming activity of ras (p. 2, lines 6-10), i.e., of serving as a tumor suppressor (as stated at p. 2, lines 22-23), while at the same time does not have lysyl oxidase enzymatic activity (p. 3, lines 26-27). Thus, therapeutic activity supported by the specification IS to inhibit In other words, the Applicants the transforming activity of ras. have determined that it is the pro-peptide portion of the initial lysyl oxidase gene (pro-enzyme) product that is responsible for the tumor suppressor activity (the "therapeutic" activity) of this the rejection for Applicants submit that Thus, gene. indefiniteness has been overcome.

Rejection under 35 U.S.C. § 112, 1st paragraph, written description

Claims 1-5 have been rejected for lack of written description support in the specification. Applicants submit that if the claims are properly parsed, it can be seen that there is no basis for a rejection for lack of written description.

1) The term "lysyl oxidase pro-peptide" is clearly defined as a structure. Lysyl oxidase pro-peptide is a portion of the product of a lysyl oxidase gene, which is cleaved off to produce the active lysyl oxidase enzyme. The identity of the pro-peptide (its sequence and, thus, its structure) is determined when the

full sequence of the gene product is determined, not just from isolating a new lysyl oxidase enzyme. Thus, the sequence (full description) of a lysyl oxidase pro-peptide from species other than the exemplary species recited in the specification will be known once the sequence of the lysyl oxidase gene has been determined in that species.

- The term "therapeutically active portion of lysyl structure. clearly defined as is oxidase pro-peptide" Applicants have discovered that the lysyl oxidase pro-peptide as a whole is "therapeutically active." (See, e.g., the experiment reported at p. 16, line 26 - p. 18, line 6.) Applicants have also described in detail how to determine smaller portions of lysyl oxidase pro-peptide that are still active therapeutically. e.g., p. 4, lines 15 - 21, and claim 6.) The "active portions" will always be of a known structure because they will have been determined systematically from a lysyl oxidase pro-peptide of known structure.
- 3) What is meant by the claim language "wherein said polypeptide does not have lysyl oxidase enzymatic activity" is clearly defined structurally. As shown by the experimental results reported herein (e.g., p. 16, line 26 p. 18, line 6), it is the lysyl oxidase pro-peptide, not the lysyl oxidase enzyme, that has the tumor suppressor activity. This "wherein" clause is simply an acknowledgement that, with the use of the term "comprising," these claims are of open form, and the claimed polypeptide can include additional amino acids, e.g., in a fusion protein. The meaning of the "wherein" clause is that whatever else the claimed polypeptide may comprise, it does <u>not</u> include an active form of a lysyl oxidase enzyme.

The term "or conservative substitutions thereof," in 4) claims 4 and 5, is clearly defined as a structure. Applicants submit that they have already shown above how a polypeptide according to claim 4 or claim 5 up to the term "or conservative substitutions thereof" is clearly described. Applicants point out that a "conservative substitution" for an amino acid is a term of The possible conservative substitutions for a given amino acid, if any, are few and are well known by the ordinary skilled Thus, the possible additional structures that are artisan. encompassed by the use of this term are also few and well known.

Applicants submit that all of claims 1-5 are clearly described, as recited above, and the rejection is overcome.

Rejection under 35 U.S.C. § 112, 1st paragraph, enablement

Claims 1-7 have been rejected as not being enabled by the Applicants submit that the arguments presented specification. above concerning written description support apply equally as well in showing that the full breadth of the claims is enabled by the teachings of the specification. Therefore, the rejection for lack of enablement is overcome.

Rejection under 35 U.S.C. § 102(b)

Claims 1-3 have been rejected as anticipated by Li et al. Applicants point out that the "lysyl oxidase polypeptide" taught in Li et al. truly is the "enzyme" portion of the proenzyme, not the pro-peptide portion as described and claimed herein. Examiner is pointed to paragraphs [0047] and [0048] of Li et al. and also, particularly, to independent claims 1, 2 and 3, where it is recited explicitly "wherein said inhibitor oxidizes said [growth factor, angiogenic factor or transactivator] at lysine

residues," or, in other words, wherein said inhibitor <u>does have</u>

<u>lysyl oxidase enzymatic activity</u>, a condition that is explicitly

<u>prohibited</u> for the Applicants' claimed invention. Thus, Li et al.

cannot anticipate the Applicants' claimed invention and the rejection is overcome.

Applicants submit that all claims are in condition for allowance and such action is requested.

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

PHILIP C. TRACKMAN et al.

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By: Holliday C. Maine, Ph.D.
Registration No. 34,346
Attorney for Applicant(s)

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
Ten Post Office Square
Boston, MA 02109
Telephone: (617) 542-2290
Telecopier: (617) 451-0313

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